

Amendments to the Claims

1. (Currently amended) ~~A light chain of a modified botulinum neurotoxin type A having a modified terminal end comprising at least one additional amino acid sequence comprising SEQ ID NO: 27~~

wherein the additional amino acid sequence comprising SEQ ID NO: 27 increases biological persistence of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional amino acid sequence comprising SEQ ID NO: 27.

2. (Currently amended) ~~The light chain of a modified botulinum neurotoxin type A of claim 1 wherein the modified terminal end is an N-terminus~~ the increased biological persistence is due to an increase in biological half-life of the modified botulinum type A neurotoxin.

3. (Currently amended) The light chain of claim 1 wherein the modified terminal end is an N-terminus, and ~~wherein the botulinum toxin is a botulinum toxin type A~~ the increased biological persistence is due to an increase in biological activity of the modified botulinum type A neurotoxin.

4-44 (Canceled)

45. (New) The modified botulinum neurotoxin type A of Claim 1, further comprising at least one additional leucine-based motif, the additional leucine-based motif comprising:

- a. a quintet comprising the first five amino acids wherein at least one amino acid is an acidic amino acid or at least one amino acid is a hydroxyl containing amino acid; and
- b. a duplet comprising two amino acids following the quintet wherein at least one of the amino acids is a leucine or at least one of the amino acids is an isoleucine; and

wherein the additional leucine-based motif increases biological persistence of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional leucine-based motif.

46. (New) The modified botulinum neurotoxin type A of Claim 48, wherein the acidic amino acid is selected from the group consisting of a glutamate, a glutamine and an aspartate.
47. (New) The modified botulinum neurotoxin type A of Claim 48, wherein the hydroxyl containing amino acid is selected from the group consisting of a serine, a threonine and a tyrosine.
48. (New) The modified botulinum neurotoxin type A of Claim 48, wherein the hydroxyl containing amino acid can be phosphorylated.
49. (New) The modified botulinum neurotoxin type A of Claim 48, wherein one amino acid of the duplet comprises a leucine, an isoleucine, a methionine, an alanine, a phenylalanine, a tryptophan or a valine.
50. (New) The modified botulinum neurotoxin type A of Claim 48, wherein the duplet comprises a leucine-leucine duplet, a leucine-isoleucine duplet, an isoleucine-leucine duplet, an isoleucine-isoleucine duplet or a leucine-methionine duplet.
51. (New) The modified botulinum toxin of Claim 1, further comprising at least one additional tyrosine-based motif, the additional tyrosine-based motif comprising four amino acids wherein the amino-terminal amino acid is a tyrosine,

wherein the additional tyrosine-based motif increases biological persistence of the modified botulinum neurotoxin type A relative to an identical botulinum neurotoxin type A without the additional tyrosine-based motif.

52. (New) The modified botulinum neurotoxin of Claim 51, wherein the tyrosine-based motif further comprises a hydrophobic amino acid at the carboxyl-terminal position.